Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/GB05/000676

International filing date: 23 February 2005 (23.02.2005)

Document type: Certified copy of priority document

Document details: Country/Office: GB
Number: 0404106.7
Filing date: 24 February 2004 (24.02.2004)

Date of receipt at the International Bureau: 07 April 2005 (07.04.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse

The Patent Office

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed

Dated   16 March 2005

Patents Form 1/77

Patents Act 1977
(Rule 16)

THE PATENT OFFICE
SW
2 4 FEB 2004
LONDON
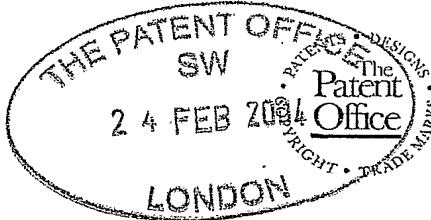
25FEB04 E875059-2 002855
P01/7700 0.00-0404106.7 CHEQUE

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

2 4 FEB 2004

The Patent Office

Cardiff Road
Newport
South Wales
NP10 8QQ

1.	Your reference	4/HH/P40099GB
2.	Patent application number *(The Patent Office will fill in this part)*	**0404106.7**
3.	Full name, address and postcode of the or of each applicant *(underline all surnames)*	SHIMADZU RESEARCH LABORATORY (EUROPE) LTD WHARFSIDE TRAFFORD WHARF ROAD MANCHESTER M17 1GP
	Patents ADP number *(if you know it)*	
	If the applicant is a corporate body, give the country/state of its incorporation	UK 7417280001
4.	Title of the invention	AN ION TRAP AND A METHOD FOR DISSOCIATING IONS IN AN ION TRAP
5.	Name of your agent *(if you have one)* "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	MATHISEN, MACARA & CO The Coach House 6-8 Swakeleys Road Ickenham Uxbridge UB10 8BZ
	Patents ADP number *(if you know it)*	1073001

6.	If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number	Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7.	If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application		Date of filing *(day / month / year)*

8.	Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:* a) *any applicant named in part 3 is not an inventor, or* b) *there is an inventor who is not named as an applicant, or* c) *any named applicant is a corporate body. See note (d))*	YES

Patents Form 1/77

9. Enter the number of sheets for any of the
   following items you are filing with this form.
   Do not count copies of the same document

   Continuation sheets of this form

   Description   12

   Claim (s)   5

   Abstract   1

   Drawing (s)   9) q ⟨ᵛ⁻)

10. If you are also filing any of the following,
    state how many against each item.

    Priority documents

    Translations of priority documents

    Statement of inventorship and right
    to grant of a patent (Patents Form 7/77)

    Request for preliminary examination
    and search (Patents Form 9/77)   1

    Request for substantive examination
    (Patents Form 10/77)

    Any other documents
    (please specify)

11.   I/We request the grant of a patent on the basis of this application.

    Signature   Mathisen, Macara   Date

    MATHISEN, MACARA & CO.   24 February 2004

12. Name and daytime telephone number of
    person to contact in the United Kingdom
                                            M. W. BIBBY (01895 678331)

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) *If you need help to fill in this form or you have any questions, please contact the Patent Office on 08459 500505.*

b) *Write your answers in capital letters using black ink or you may type them.*

c) *If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.*

d) *If you have answered 'Yes' Patents Form 7/77 will need to be filed.*

e) *Once you have filled in the form you must remember to sign and date it.*

f) *For details of the fee and ways to pay please contact the Patent Office.*

1

AN ION TRAP AND A METHOD FOR DISSOCIATING
IONS IN AN ION TRAP

This invention relates to an ion trap and a method for dissociating ions in an
5   ion trap, and relates especially to a quadrupole ion trap and to tandem mass
analysis using a quadrupole ion trap.

Tandem mass analysis can be achieved by employing an ion trap analyser,
which may be in the form of a magnetic cyclotron (FTICR MS) or a high
frequency quadrupole ion trap. In a tandem mass spectrometer, a precursor ion
10   with a certain mass to charge ratio is selected and is isolated inside the trapping
volume. A dissociation procedure then follows using one of a number of known
activation methods, including collision induced dissociation (CID), surface
induced dissociation (SID), infrared multi-photon dissociation (IRMPD) and
electron capture dissociation (ECD). The product ions resulting from this
15   procedure are measured using a mass scan to obtain an MS^2 spectrum. If a further
precursor ion is selected from the product ions and the dissociation procedure
repeated the subsequent mass scan will give an MS^3 spectrum. Such a time
domain procedure can be repeated to generate MS^n spectra. The capability of a
tandem mass spectrometer is very important, as MS^n spectra allow for the
20   elimination of chemical noise while, at the same time, increasing confidence in the
identification of the chemical structure of the original ions by detecting and
analysing specific product ions. This kind of tandem mass analysis is also
efficient in elucidating and sequencing complicated molecular structures, such as
protein and DNA.

25   Of the above dissociation methods, ECD was developed most recently and
offers more extensive sequence information. For peptide and protein sequencing,
ECD results in the backbone bond cleavage to form a series of c-type and z-type
ions. This is in contrast to the commonly used CID which is only capable of

cleaving the weak peptide bonds to form b-type and y-type ions resulting in loss of labile post-translational modification.

However, ECD has only been implemented using the FTICR mass spectrometer. While the quadrupole ion trap has been used for tandem mass analysis employing CID, and IRMPD to fragment protein or peptide ions, the quadrupole ion trap has not hitherto successfully incorporated ECD. It is likely that this is for the following reasons:

1. For ECD, the kinetic energy of electrons must be very low, typically around 0.2eV. It is very difficult to transfer such low energy electrons from an electron source to the ion trapping region. In FTICR, where a strong magnetic field is employed a low energy thermo-emitted electron is always focused and is guided by the magnetic field lines until it reaches the trapping region. In the case of quadrupole ion trap, where a strong time-varying electric field is used to confine ions, the electric field will either accelerate or retard injected electrons. If a sinusoidal RF voltage is used to generate the trapping electric field, there is hardly any practical time window within which electrons can be injected and reach the centre of the ion trap with the required kinetic energy. Injected electrons are either accelerated to higher energies or simply ejected by the electric field. Fragmentation, due to these high-energy electron impacts masks the useful information obtained from ECD and it is very difficult to gate the injection of electrons to coincide with the narrow time window when the RF trapping voltage has the correct phase.

2. The mechanism of electron capture dissociation requires both the creation and preservation of the so-called Rydberg state of precursor ions according to current theoretical models of ECD. However, high electric fields within the quadrupole ion trap tend to destroy Rydberg states causing removal of electrons from the Rydberg orbit to a continuum. Even in the central region of the ion trap (the ion cloud may occupy a space over 2 mm in diameter) the field

intensity may still cause a loss of the intermediate excitation state, with a consequent reduction in the efficiency of ECD.

3. It is common to use buffer gas in the ion trap to cause collisional cooling. The buffer gas pressure is normally at a pressure around 10^{-3} mbar and hundreds of collisions per millisecond will occur between the trapped ions and the buffer gas. Such collisions with the buffer gas in an ion trap can also destroy Rydberg states, which in turn reduces the efficiency of ECD.

Nevertheless, implementation of ECD in a quadrupole ion trap offers an attractive approach due to the fact that the quadrupole ion trap mass spectrometer is much cheaper to build compared with the FTICR instrument. US patent 6,653,662 B2, Jochen Franzen discloses procedures for the implementation of ECD in a 3 D RF quadrupole ion trap. The method includes injecting electrons through an aperture in the ion trap electrode carrying the RF voltage, whereby the electron source is kept at the highest positive potential achieved at the centre of the ion trap during the RF cycle. With this method, electrons can reach the centre of the trap, interacting with the stored ions for a period of a few nanoseconds, while satisfying the low energy requirement of ECD. Although this method overcomes the first problem listed above, it results in a very narrow time window within which the electron beam can irradiate the trapped ions. It had been anticipated that the injected electrons would be captured by the potential well of the entire ion cloud and thereby survive and accumulate over successive RF cycles. However, such expectations have neither theoretical nor experimental support.

ECD is used to dissociate multiply-charged positive ions and is one example of electron induced dissociation. In another example of electron induced dissociation, electrons are injected into the ion trap to dissociate negative ions.

According to one aspect of the invention there is provided a method for dissociating ions in an ion trap, comprising the steps of switching a trapping voltage between discrete voltage levels to create a digital trapping field for trapping precursor ions and product ions in a trapping region of the ion trap, and

injecting electrons into said ion trap while the trapping voltage is at a selected said voltage level whereby injected electrons reach the trapping region with a kinetic energy suitable for electron induced dissociation to take place.

According to another aspect of the invention there is provided an ion trap

5   including switch means for switching a trapping voltage between discrete voltage levels to create a digital trapping field for trapping precursor ions and product ions in a trapping region of the ion trap, a source of electrons and control means for causing source electrons to be injected into said ion trap while the trapping voltage is at a selected one of said voltage levels whereby the injected electrons reach the

10   trapping region with a kinetic energy suitable for electron induced dissociation to take place.

The invention makes possible an extension of the time window within which low energy electrons can reach the ion cloud at the centre of the ion trap for effective ion electron interaction. The invention also makes it possible to reduce

15   the electric field strength while maintaining ions in the trapping region during the dissociation process.

The pressure of buffer gas in the trapping region may be reduced to preserve the required intermediate state of ions during the ECD process.

20   In order to extend the time window for ECD, the conventional sinusoidal RF trapping waveform must be modified. GB 1346393 discloses a quadrupole mass spectrometer that is driven by a periodic rectangular or trapezoidal waveform. WO 0129875 further discloses a digital ion trap driving method, where the trapping field is driven by a voltage which switches between high and

25   low voltage levels. This trapping method offers an opportunity for injecting electrons into the trapping region and allowing them to interact with the trapped ions.

In a preferred embodiment of the invention, the ion trap includes means for generating a magnetic field for guiding injected electrons to the trapping region.

Embodiments of the invention are now described by way of example only, with reference to the accompanying drawings, of which:

Figure 1 illustrates a quadrupole ion trap in which ECD can take place,

Figure 2 shows the waveform (referenced 1) of the RF drive voltage applied to the ion trap and the waveform (referenced 2) of the pulsed gating voltage applied to an electron emitter during the ECD process,

Figure 3 is a simulation illustrating injection of electrons into a 3D ion trap. The initial electron energy is 1 eV and is reduced to 0.2~0.7 eV upon reaching the central region of ion trap,

Figure 4 shows the waveform of an RF drive voltage having three discrete voltage levels.

Figure 5 shows a switching circuit for implementing the three-level drive voltage of Figure 4,

Figure 6(a) and 6(b) illustrate the application of magnetic field to assist electron injection. Figure 6(a) shows the electron beam being injected with reduced energy through a hole in an end cap electrode and Figure 6(b) shows the electron beam being introduced through a hole in the ring electrode.

Figure 7 illustrates a linear quadrupole ion trap in which ECD can take place.

Figure 8 illustrates waveforms of the RF drive voltage applied to X and Y electrodes of a linear ion trap.

Figure 9(a) illustrates an implementation of ECD in a linear quadrupole ion trap and Figure 9(b) illustrates the variation of DC voltage along the axis of the linear quadrupole ion trap.

Figure 1 of the accompanying drawings shows one implementation of the invention in which the ring electrode 7 of a 3D ion trap is connected to a pair of switches 1, 2. The switches 1, 2 are electronic switches that are connected

together in series as shown in figure 1. In this embodiment, switch 1 is connected to a high level DC power supply 4 and switch 2 is connected to a low level DC power supply 5. The switches are turned on and off alternately creating a rectangular waveform drive voltage which is applied to the ring electrode 7 of the

5   quadrupole ion trap. The quadrupole ion trap has at least one hole in the ejection end cap electrode 8 through which ions can be ejected to an off-axis detector 10 via an extraction electrode 9. The off-axis detector comprises a conversion dynode 10a and an electron multiplier 10b. When the ECD process is activated, a high voltage bias on the detector 10 is switched off and an electron emitter 11 is

10   turned on. A pulsed electron beam 15 is generated by controlling a pulsed gate voltage applied to gate 12. Waveform 1 of Figure 2 shows the timing of the drive voltage applied to the ring electrode 7, whereas waveform 2 of Figure 2 shows the timing of the pulsed gate voltage applied to gate electrode 12. The potential at centre of the ion trap where the trapped ions accumulate is also represented by the

15   dashed line 3. Referring to figure 1, an electron beam 15 is produced when the voltage on ring electrode 7 undergoes a negative excursion, for example at -500 V. In the case of an ion trap having a theoretical geometry, i.e. $r_0 = 1.414 z_0$, the potential at the centre of the ion trap is -250V. The electron emitter 11 is also biased with a voltage of -250V and electrons will be accelerated to 250 eV when

20   they approach the hole in the end cap electrode 8, thereby making it easier to pass through the hole. After the electrodes have entered the ion trap they are retarded by the "static" quadrupole field. This is because electron motion is relatively fast compared with the microsecond time interval needed for switching. Within nanoseconds, electrons reach the central region of the ion trap but have lost most

25   of their kinetic energy and can be captured by a trapped multiply charged ion. Figure 3 shows a simulation of 4 electrons injected into the ion trap in the above described manner. The electrons generated by the emitter 11 at -249V start with an initial kinetic energy of 1eV and initial angles of up to 88 degrees (i.e. nearly all possible angles) with respect to the ion trap axis. The radius of the range of

emission points is between 0 and 0.6mm. Once the electrons have entered the ion trap they are strongly focused in the transverse directions.

It is easier to inject electrons through end cap electrode 8 than through the ring electrode 7. This is because in the latter case, electrons are not focused in all
5   transverse directions i.e. only in the axial direction of the ion trap, but not in the direction perpendicular to the trap axis.

Application of a digital trapping voltage, as described, enables the time window within which ECD can take place to be extended, and so gating of the electron beam becomes relatively straightforward. Therefore there is no longer any
10   requirements to inject ions through the electrode to which the trapping voltage is applied, in order to prevent high energy electrons from reaching the trapping centre and hitting the ion cloud, as taught by US Patent No. 6,653,662. However, injection through ring electrode 7 also has other advantages as now explained.

Many prior art implementations demonstrate that ECD product ion intensity
15   does not increase in proportion to the exposure time to electrons. Over-exposure causes decreased intensity of product signals with the parent ion peak being much higher than the peaks of the product ions. This is due to neutralization of product ions by subsequent capture of electrons. However, the product ions can be removed from the ion electron interaction region if an appropriate excitation
20   waveform is applied. If electrons are injected through the ring electrode of a quadrupole ion trap, as mentioned above, the electrons are focused in the z-direction and reach the ion cloud in the centre of the x-y plane. Ions can be selectively removed from this plane by applying a dipole tickling voltage across the end cap electrodes. When the mass-to-charge ratio of the precursor ions has
25   been selected, a notch-filtered broad band excitation waveform can be readily created with the notch frequency assigned to the secular frequency of the precursor ion. When the excitation waveform is applied to the end cap electrodes, all ions except the precursor ion will be removed from the centre plane where electron irradiation occurs. By such means, the product ions produced by the ECD process

will be removed from the centre of the ion trap and so protected from a cascading decay, and useful product ions may be accumulated.

Each successive period selected for electron irradiation should preferably be at least as long as the period when there is no irradiation. This creates a relatively wide time window during which ECD can take place and also gives rise to a relatively low absolute trapping voltage value, since the average DC potential over the whole period is normally zero in order to provide the widest mass trapping range. When a lower trapping voltage is used during the ECD process, the better the chance to preserve the Rydberg state. Therefore, ECD efficiency can be improved when the rectangular waveform voltage is lower and a longer excursion of the waveform is used for ion electron interaction.

In order to further reduce the field strength for ECD to take place and yet, at the same time, maintain a sufficient trapping force, a 3 level digital waveform can be used. Such a waveform is shown in figure 4, and figure 5 illustrates a switching circuit which can be used to generate such a waveform. In this alternative embodiment, switch 51 is connected to a high level DC power supply 54 and switch 53 is connected to a low level DC power supply 56. An additional switch 52 is connected between a middle level DC power supply 55 and the junction of power supplies 54,56. The middle level DC power supply 55 may have a voltage in the range of 0 to -100V. When the three switches are turned on and off sequentially, the resultant output voltage will have a stepped waveform as shown in figure 4. The electron beam is activated and injected into the trap during each middle level excursion 42. Because of the very low electric field in the trapping region of the ion trap, the resultant intermediate state of excited ions will not be damaged before dissociation starts.

Unless there is a sufficient retarding field for reducing the energy of electrons in the trapping region, the electrons must be injected into the trapping region with very low kinetic energies. Focusing a low energy electron beam at the

centre of the ion trap is very difficult, with the result that many electrons may not reach the centre of the ion trap where interaction with the trapped ions takes place. With a view to alleviating this problem, a magnetic field is applied to the ion trapping region. Calculation shows that a magnetic field of less than 150 Gauss

5   will be sufficient to confine an electron beam generated by a thermo cathode to a beam within 1mm diameter. This easily enables the electron beam to overlap and interact with the ion cloud in the ion trap. As shown in figure 6a, the magnetic field can be generated by a coil 60 surrounding the ion trap. The product of the number of turns and current is about 2000 A. The resultant magnetic field

10   intensity has a negligible effect on ion trapping and can be switched off during precursor isolation and mass scanning.

A magnetic field may also be used to focus an electron beam injected through a hole in the ring electrode. By this means, divergence in the x-direction at the centre of the x-y plane can be reduced and efficiency of ECD increased.

15   Figure 6b shows an arrangement for creating a magnetic field of this kind. As shown, Hemholtz type coils 61 and 62 may be used to generate the magnetic field within the ion trapping region.

A linear quadrupole ion trap may also be driven by a switching circuit and this has been disclosed in WO0129875. As in the case of a 3D ion trap, a digitally

20   driven linear ion trap also opens up the opportunity for ECD to take place. One of the ways to drive the linear ion trap is shown in figure 7. One pair of switches 73 is connected to the pair of X electrodes 72 and another pair of switches 74 is connected to the pair of Y electrodes 71. When the switch pairs 73, 74 operate alternately between a high voltage level V_H and a low voltage level V_L , each

25   outputs a rectangular waveform to the respective electrode pair 72, 71. An additional circuit 75 may be used to generate a dipole field within the trapping volume to cause resonance excitation of ions which is needed for mass selective isolation, CID and mass scanning. Figure 8 shows three examples of a rectangular waveform applied to the X and Y electrode pairs. In the first example, (a), the two

rectangular wave voltages 1 and 2 are in anti-phase. The resultant quadrupole field 3 created in the trapping volume also has a rectangular waveform. Under such conditions, ions can be trapped and selected using methods already disclosed in the prior art; however, an electron would be easily deflected if it travels along

5 the axis of the linear ion trap. In the second and third examples, (b) and (c), the rectangular wave voltages applied to the X electrodes and Y electrodes are generated with relative phase shifts rather than in anti phase. This causes the electric field inside the trapping volume to have a stepped waveform 6 or 9, which includes at least one zero field excursion. In configuration (b) the zero field

10 excursion occurs only once during each period, when both X and Y electrodes are connected to the higher voltage level. In configuration (c) the zero field excursion occurs twice during each period, once when both the X and Y electrode pairs are connected to the higher voltage level, and once when both the X and Y electrode pairs are connected to the lower voltage level. During the zero field excursion,

15 electrons with very low kinetic energy may travel along the axis without acceleration or deflection in the X or Y direction. With the assistance of a magnetic field directed along the trap axis, the electron beam is expected to overlap with the ion cloud enabling ECD to take place. Configuration (b) may offer a larger ECD time window than configuration (c); however, the average

20 potential on the trap axis is no longer zero volts since an asymmetric rectangular waveform is being used (duty cycle >0.5). This may cause some difficulties in designing the DC stopping potential at the two ends of the linear ion trap. With configuration (c) the average DC voltage is zero volts and so conventional methods for applying a DC stopping field can be used. The time interval when

25 both pairs of electrodes are at the higher voltage level, as marked with a shadowed box 10 on the time axis, is preferred for the injection of the electron beam. This embodiment is depicted in brief in Figures 9a and 9b.

Figure 9a is a schematic diagram showing a linear ion trap in combination with an electron source for ECD. In this configuration, the linear ion trap has a

front segment 93, a main segment 91 and a back segment 92. Ions can be introduced via a gate 94 and the front segment 93 where they enter the main segment 91 and finally form a linear ion cloud 90. Figure 9b shows the DC potential along the axis of the ion trap at the moment of electron injection, and this

5 corresponds to interval 10 in Figure 8b and 8c. Only during this excursion, can electrons from source 11 be injected from the right hand end entrance 95 and enter the trap segments 92, 91 and 93. At the left hand end, electrons will be reflected and will re-enter the interaction region. Since the electrons are expected to travel along the trap axis within the trapping volume with a very low energy, a magnetic

10 field is used to guide the electron beam. This magnetic field is generated by a pair of Hemholtz coils 96 and 97. The position of the coils must be adjusted to align the magnetic field so as to be parallel to the axis of the linear ion trap. As mentioned above for a 3D ion trap, a dipole field can be used to remove product ions from the central region of the ion trap. This will prevent cascading

15 neutralization of the product ions thereby improving ECD efficiency.

A pulsed gas injection is needed to cool down the ion motion before ECD takes place. Buffer gas, having a constant high pressure, may reduce the efficiency of ECD so it is not recommended. The timing of a pulsed valve which introduces buffer gas into the trapping region must be synchronised with the ECD

20 timings (waveform changing, electron gating and coil charging) to allow sufficient pumping out time before ECD starts.

In the case of a linear ion trap, substantial damping of the kinetic energy of ions may take place in one linear ion trap having a relatively high gas pressure, while ECD may take place in another, down stream linear ion trap where the gas

25 pressure is lower. An orifice between the two ion traps may be used to maintain the pressure differential.

The methods disclosed here are only examples. Various configurations can be designed to carry our ECD with a 3D or a linear ion trap driven by a digital

trapping voltage. For example, the electron source may be arranged off-axis, or may be designed to have a ring or hollow shape, enabling a laser beam to impinge on the ion cloud, as may be needed for other ionisation or dissociation purposes. The ion trap incorporating ECD according to the invention may be a stand alone

5   mass spectrometer or may form part of a tandem mass spectrometer, such as in an ion trap – time of flight hybrid system.

CLAIMS

1. A method for dissociating ions in an ion trap, comprising the steps of switching a trapping voltage between discrete voltage levels to create a digital trapping field for trapping precursor ions and product ions in a trapping region of the ion trap, and injecting electrons into said ion trap while the trapping voltage is at a selected said voltage level whereby injected electrons reach the trapping region with a kinetic energy suitable for electron induced dissociation to take place.

2. A method as claimed in claim 1 wherein the initial kinetic energy of the injected electrons is reduced to said kinetic energy suitable for electron induced dissociation to take place after the electrons have entered the ion trap.

3. A method as claimed in claim 2 wherein said trapping voltage is switched between two discrete voltage levels.

4. A method as claimed in claim 1 wherein the electrons have a relatively low initial kinetic energy substantially suitable for electron induced dissociation, and are injected into said trapping region while the trapping voltage is at or close to zero volts.

5. A method as claimed in claim 4 wherein the trapping voltage has three discrete voltage levels and electrons are injected into said trapping region while the trapping voltage has the lowest absolute voltage value.

6. A method as claimed in any one of claims 1 to 5 including using a magnetic field to guide injected electrons to the trapping region.

7. A method as claimed in claim 6 wherein said magnetic field is generated using an electrical coil arranged to be energised by a pulsed current.

8. A method as claimed in any one of claims 1 to 7 wherein the ion trap is a 3-D quadrupole ion trap and electrons are injected into the trapping region through a hole in an end cap electrode of the ion trap.

9. A method as claimed in any one of claims 1 to 7 wherein the ion trap is a 3-D quadrupole ion trap and electrons are injected into the trapping region through a hole or slit in the ring electrode of the ion trap.

10. A method as claimed in any one of claims 1 to 7 wherein the ion trap is a linear quadrupole ion trap.

11. A method as claimed in claim 10 wherein electrons are injected along the longitudinal axis of the ion trap from one end of the trapping region.

12. A method as claimed in any one of claims 1 to 11 including introducing pulses of gas into the trapping region of the ion trap to cause collisional cooling of ions prior to or after dissociation.

13. A method as claimed in claim 12 wherein said pulses of gas are introduced into the trapping region using a pulsed valve and a vacuum pump capable of rapidly reducing the gas pressure to below 10^{-4}mbar.

14. A method as claimed in any one of claims 1 to 13 including applying a pulsed gate voltage to gating means to control extraction of electrons from an electron source for injection into said trapping region and synchronising

application of said pulsed gate voltage with the step of switching said trapping voltage to said selected voltage level.

15. A method as claimed in any one of claims 1 to 7 including applying a broadband dipole signal to the ion trap to remove product ions from the central region of the ion trap.

16. A method as claimed in any one of claims 1 to 15 wherein the trapped precursor ions include multiply-charged precursor ions, and the injected electrons have a kinetic energy less than 1eV and are capable of inducing electron capture dissociation of said multiply-charged ions.

17. An ion trap including switch means for switching a trapping voltage between discrete voltage levels to create a digital trapping field for trapping precursor ions and product ions in a trapping region of the ion trap, a source of electrons and control means for causing source electrons to be injected into said ion trap while the trapping voltage is at a selected one of said voltage levels, whereby the injected electrons reach the trapping region with a kinetic energy suitable for electron induced dissociation to take place.

18. An ion trap as claimed in claim 17 wherein said switch means is arranged to switch said trapping voltage between two discrete voltage levels.

19. An ion trap as claimed in claim 17 wherein said electrons have a relatively low initial kinetic energy substantially suitable for electron induced dissociation to take place and the electrons are injected into said trapping region while the trapping voltage is at or close to zero volts.

20. An ion trap as claimed in claim 19 wherein said switch means is arranged to switch said trapping voltage between three discrete voltage levels and said control means is arranged to cause injection of said electrons into the trapping region while the trapping voltage has the lowest absolute voltage value.

21. An ion trap as claimed in any one of claims 17 to 20 including means for generating a magnetic field for guiding injected electrons to the trapping region.

22. An ion trap as claimed in claim 21 wherein said means for generating a magnetic field comprises an electrical coil and means for energising the coil with pulsed current.

23. An ion trap according to any one of claims 17 to 22 in the form of a 3-D quadrupole ion trap, wherein electrons are injected into the trapping region through a hole or slit in an end cap electrode of the ion trap.

24. An ion trap according to any one of claims 17 to 22 in the form of a 3-D quadrupole ion trap, wherein electrons are injected into the trapping region through a hole or slit in the ring electrode of the ion trap.

25. An ion trap according to any one of claims 17 to 22 in the form of a linear quadrupole ion trap.

26. An ion trap according to claim 25 wherein electrons are injected along the longitudinal axis of the ion trap from one end of the trapping region.

27. An ion trap according to any one of claims 17 to 25 including a gas source for introducing pulses of gas into the trapping region to cause collisional cooling of ions prior to or after dissociation.

28. An ion trap as claimed in claim 27 wherein the gas source includes a pulsed valve and a vacuum pump capable of rapidly reducing gas pressure to below 10^{-4} mbar

29. An ion trap as claimed in any one of claims 17 to 28 wherein said control means includes gating means, means for applying a pulsed gate voltage to said gating means to control extraction of electrons from a said source of electrons, and means for synchronising application of said pulsed gate voltage with the switching of said trapping voltage to the selected voltage level.

30. An ion trap as claimed in any one of claims 17 to 22 including means for applying a broadband dipole signal to the ion trap to remove product ions from the central region of the ion trap.

31. A method of dissociating ions in an ion trap substantially as herein described with reference to the accompanying drawings.

32. An ion trap substantially as herein described with reference to the accompanying drawings.

33. A tandem mass spectrometer including an ion trap as claimed in any one of claims 17 to 30 and claim 32.

18

ABSTRACT

AN ION TRAP AND A METHOD FOR DISSOCIATING IONS IN AN ION TRAP

5

A quadrupole ion trap includes a switch 3 for switching a trapping voltage between discrete voltage levels V_H, V_L. This creates a digital trapping field for trapping precursor ions and product ions in a trapping region of the ion trap. A

10   gating voltage is applied to a gate electrode 12 to control injection of source electrons into the ion trap. Application of the gating voltage is synchronised with the switching so that electrons are injected into the trapping region while the trapping voltage is at a selected one of the voltage levels and can reach the trapping region with a kinetic energy suitable for electron capture dissociation

15   to take place.

FIGURE 1

Figure 2

| 0V | -500V | 0V | -60V | 1000V | 0V | - 249V |

Figure 3

Figure 4

Figure 5

60

FIGURE 6 a

11

11

61

FIGURE 6 B

62
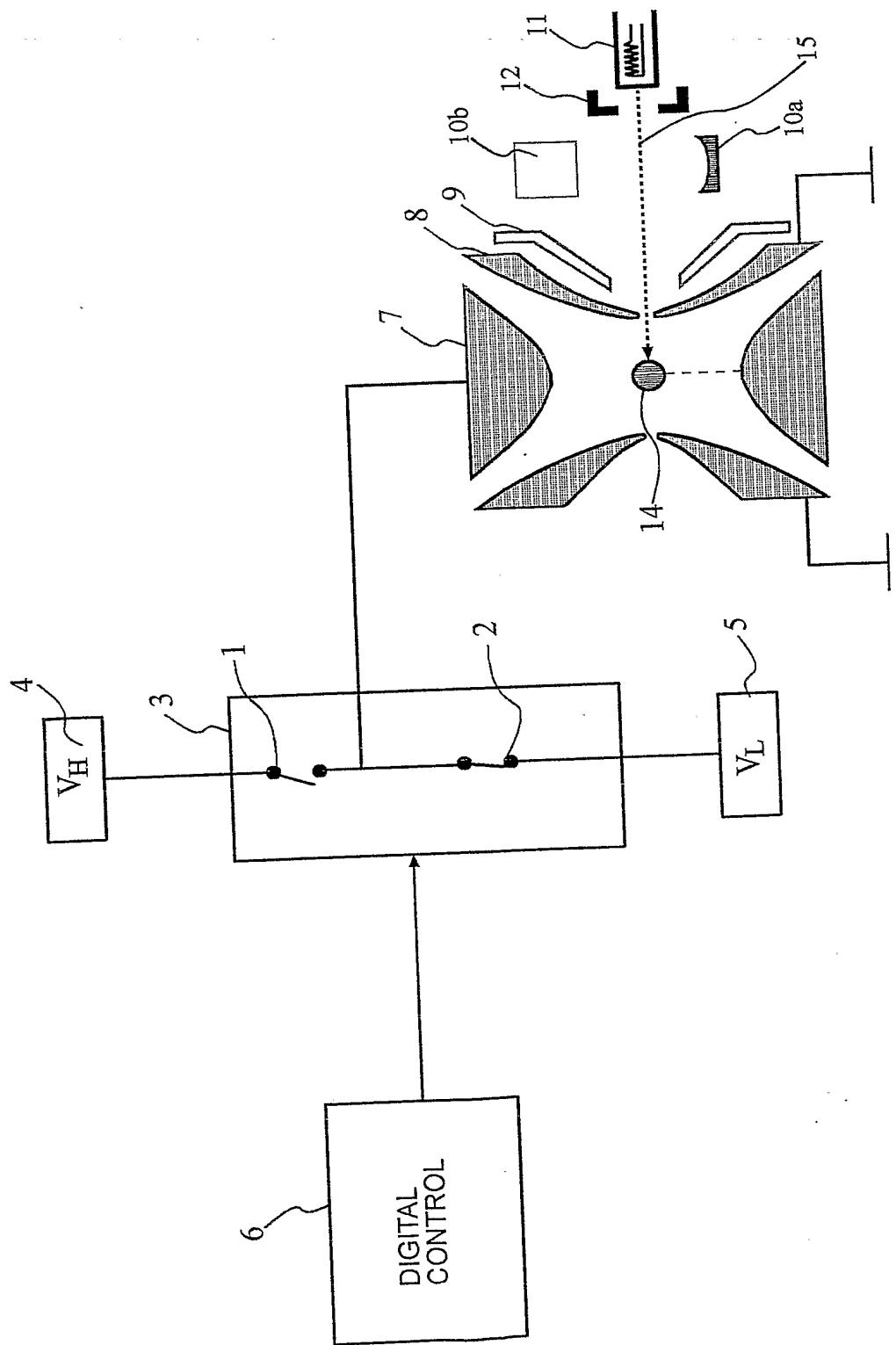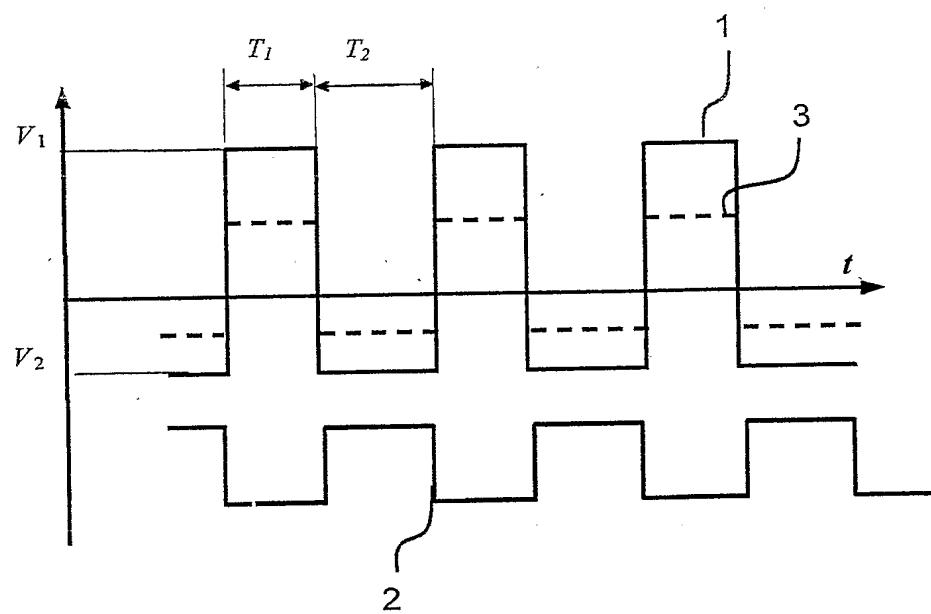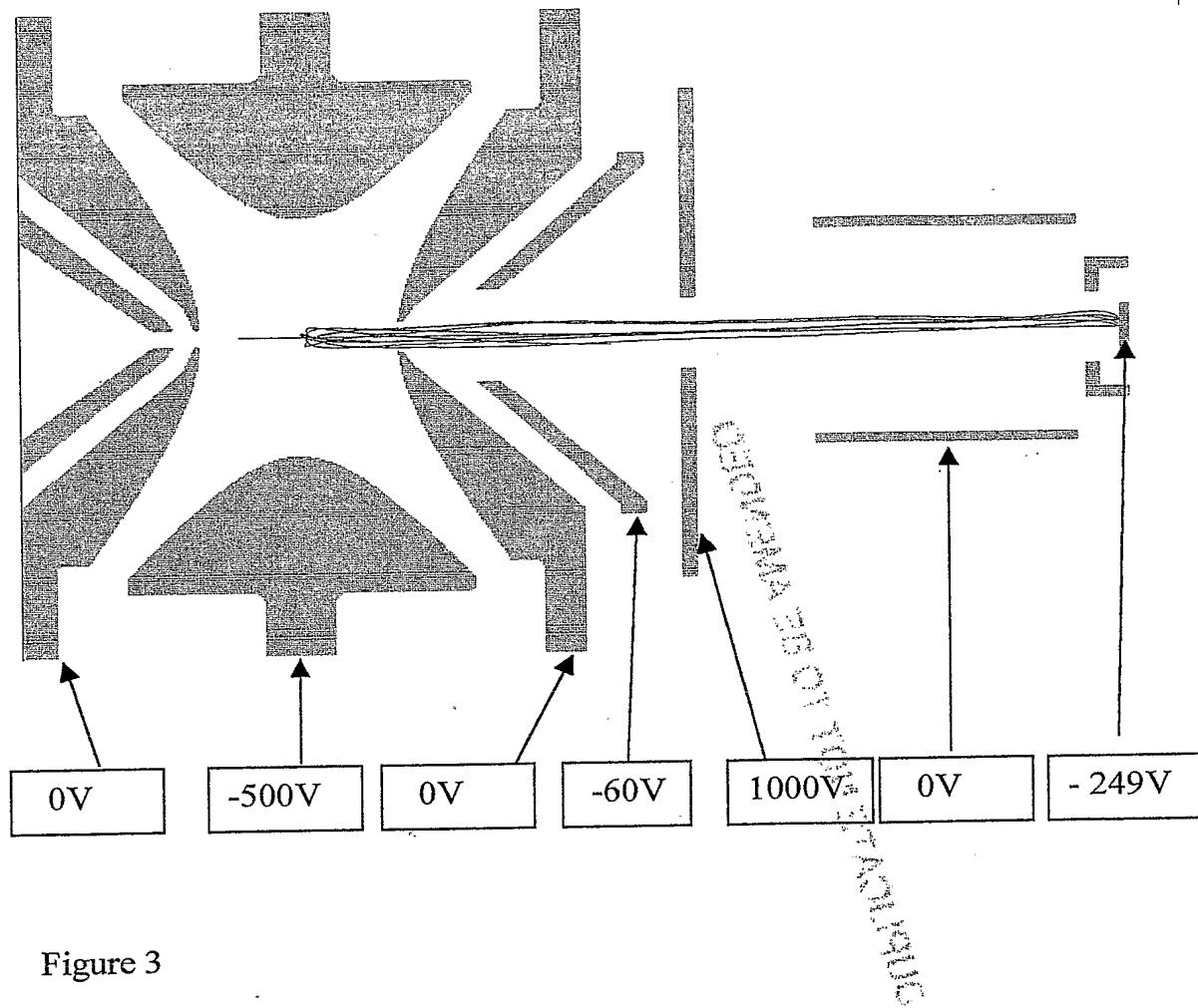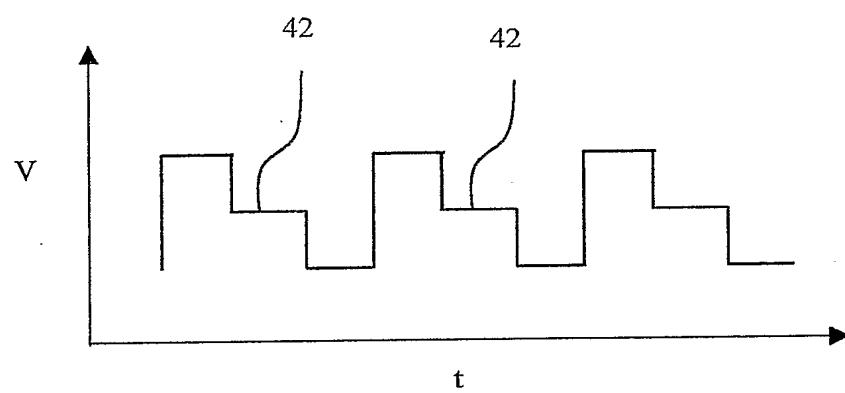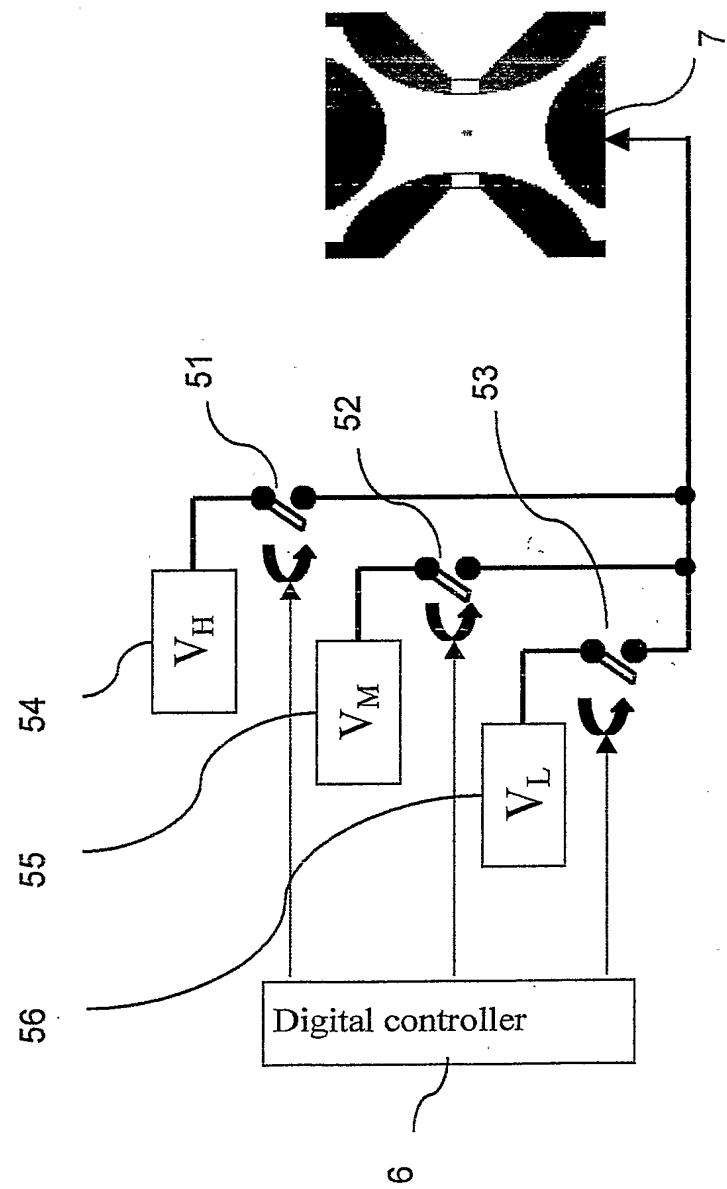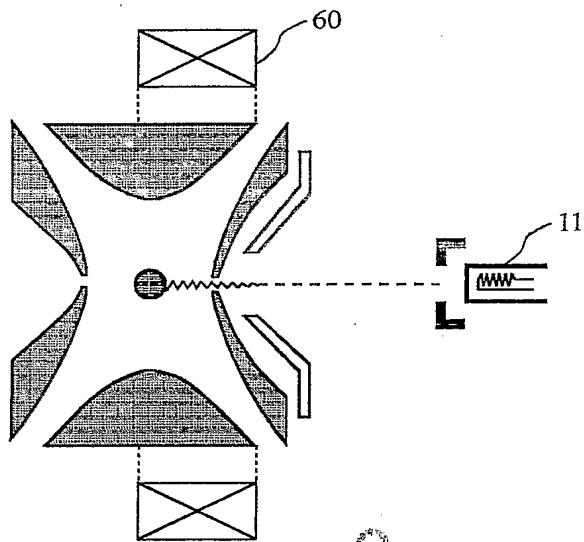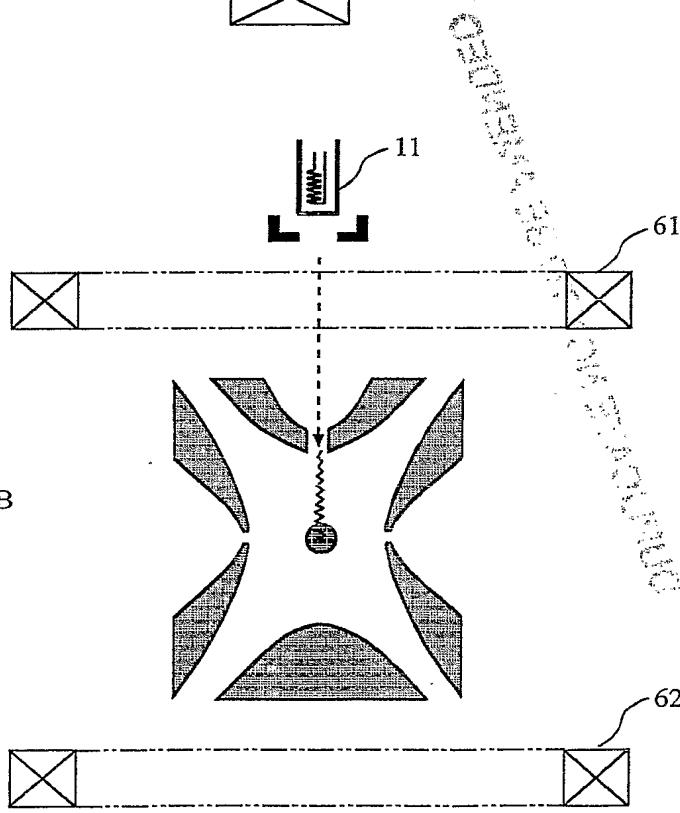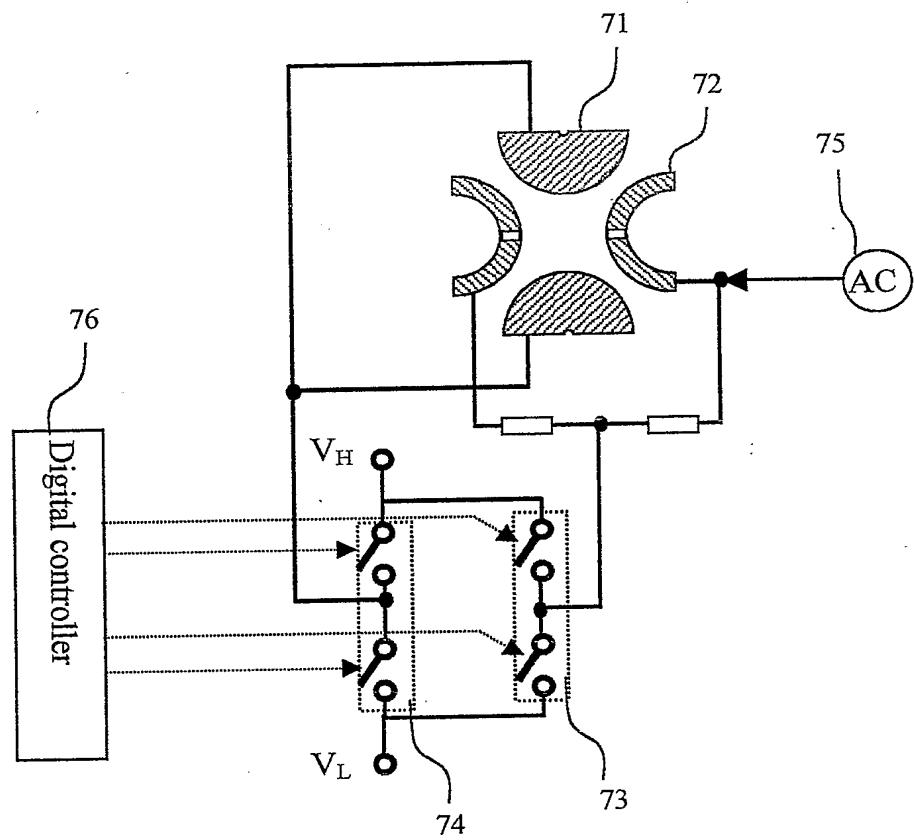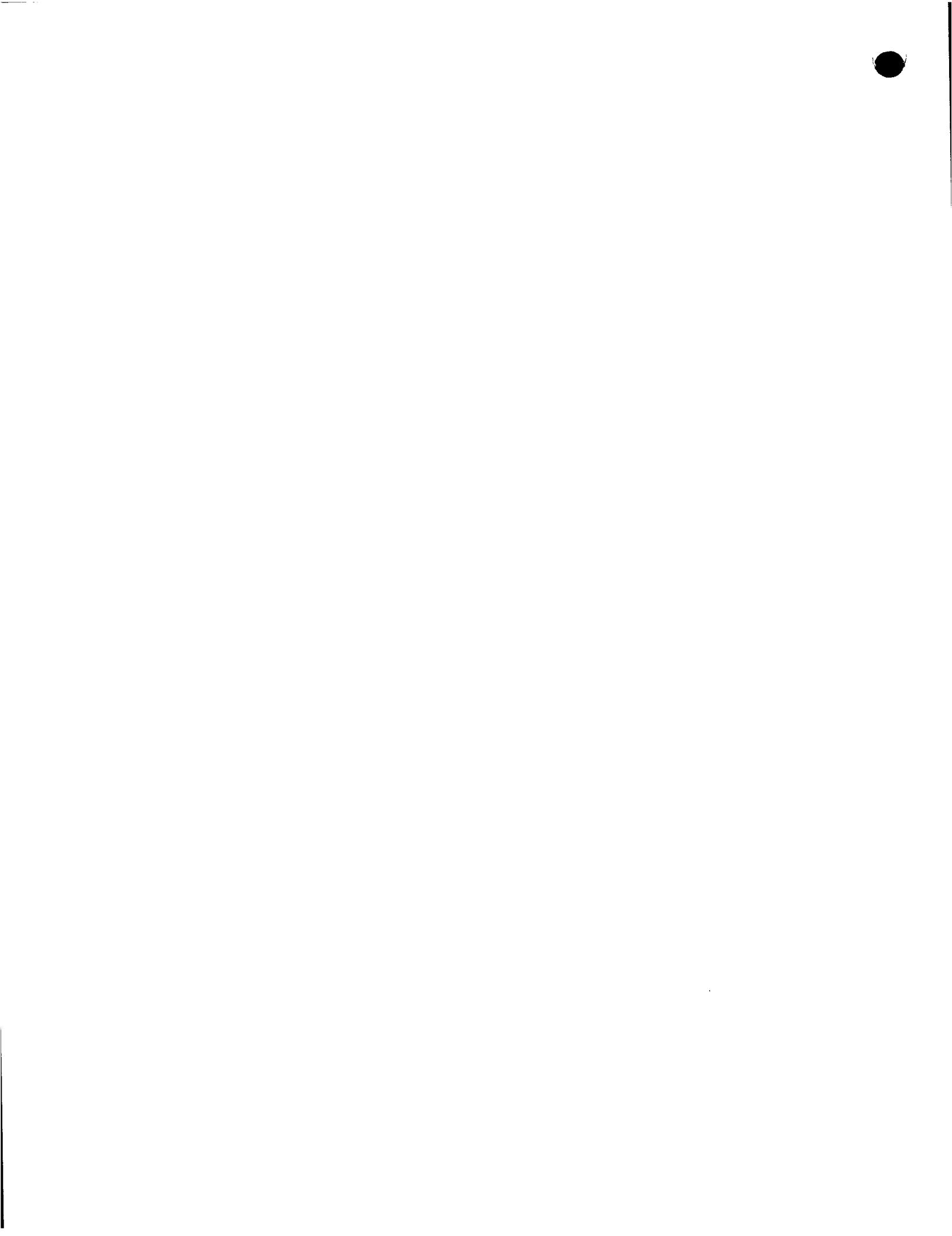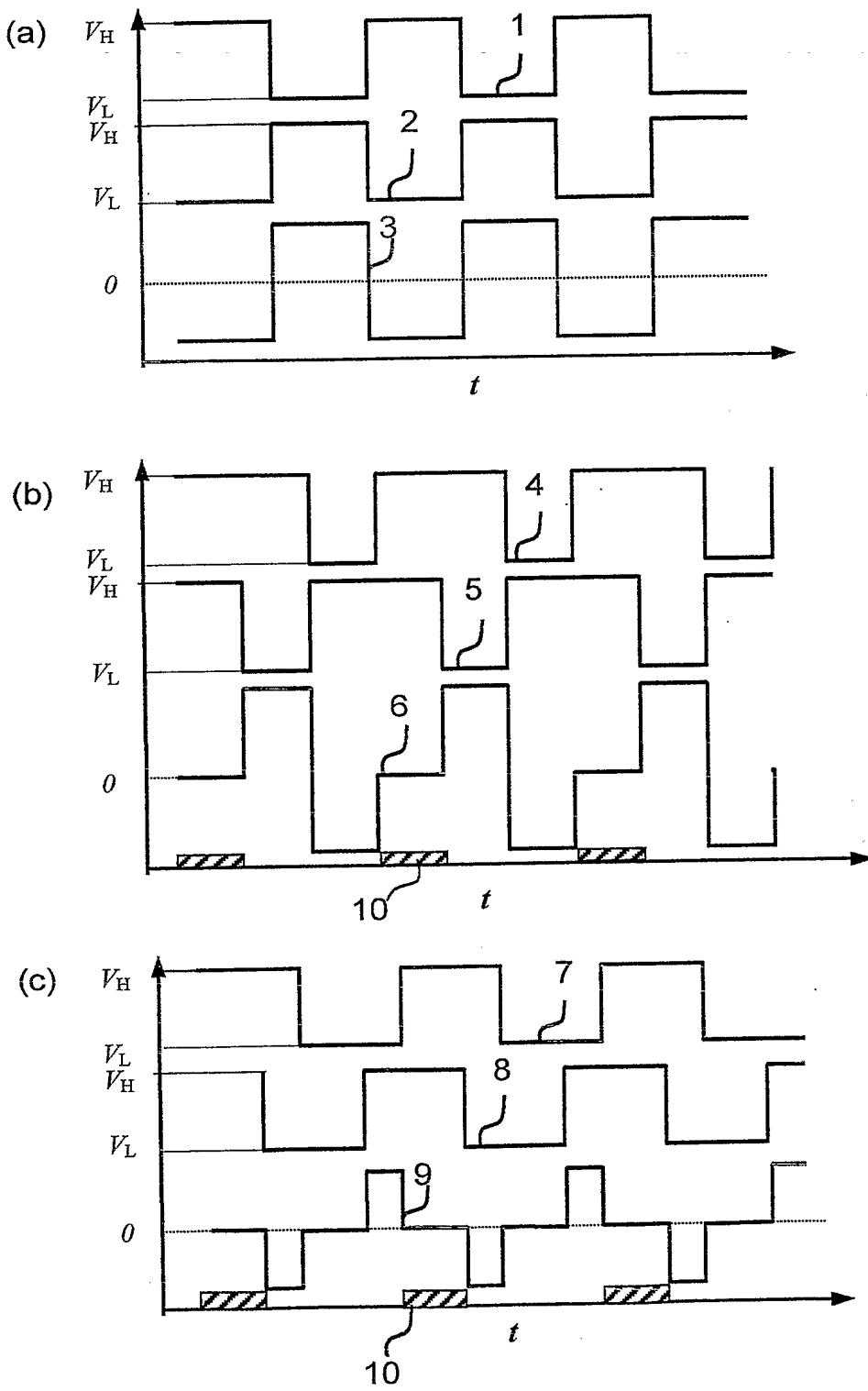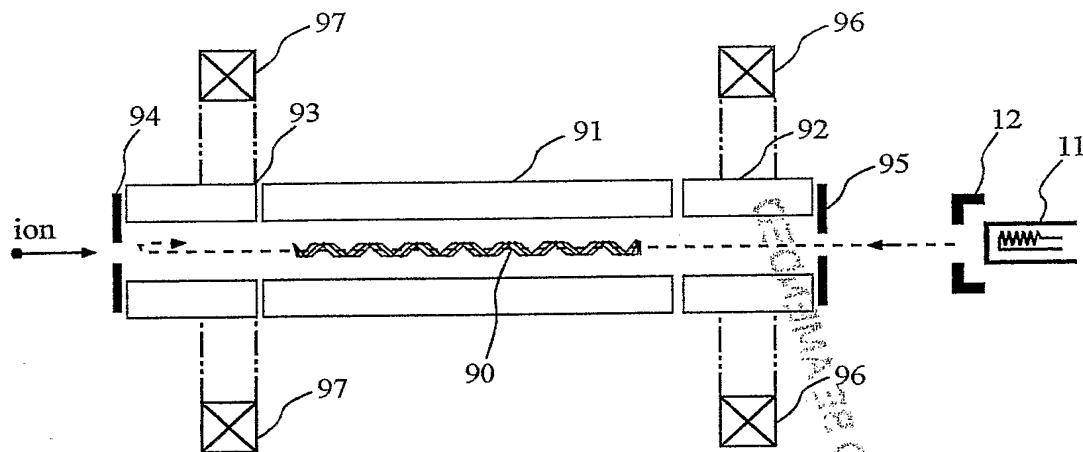
Figure 7

Figure 8

FIGURE 9a
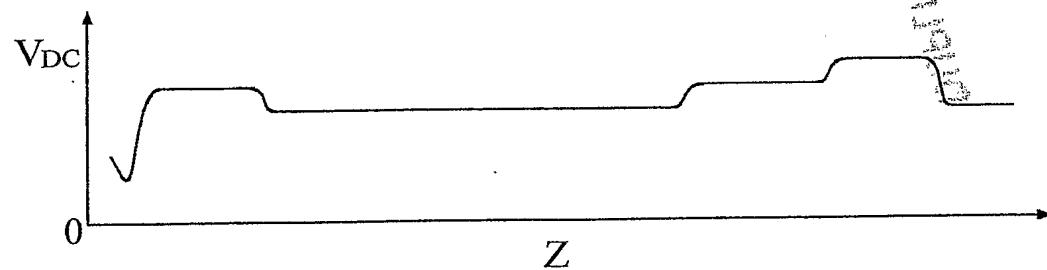
FIGURE 9b

PCT/GB2005/000676.

PCT/GB2005/000676.